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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/673,884	ASADA ET AL.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18,31,34,36 and 38-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,18,31,34,36 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/06;2/20/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed February 20, 2007. Claims 16, 18, 31, 34, 36 and 38-45 were previously pending. Applicants amended claims 16, 18, 31, 36, 39 and 43. Claims 16, 18, 31, 34, 36 and 38-45 are pending and will be examined.

2. Applicants' amendments overcame the following rejections: rejection of claims 16, 18, 40-42 and 45 under 35 U.S.C. 102(b) as anticipated by Miura et al.; rejection of claims 31, 34, 36 and 38 under 35 U.S.C. 103(a) over Miura et al. and Stratagene Catalog. All other rejections are maintained for reasons given in the "Response to Arguments" section below.

Terminal Disclaimer

3. The terminal disclaimer filed on February 20, 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of the U.S. Patent No. 6,673,578 has been reviewed and is accepted. The terminal disclaimer has been recorded. The terminal disclaimer obviated the non-statutory obviousness-type double patenting rejection of claims 16, 18 and 39 over claim 7 of the U.S. Patent No. 6,673,578.

4. Applicants' assertion that the application No. 10/435,633 is abandoned is insufficient to obviate the provisional obviousness-type double patenting rejection of claims 16, 18, 31, 36, 39 and 43 over claims 10-17 of the application No. 10/435,633, since the case has not been abandoned.

5. This office action is made non-final because of new grounds for rejection (35 U.S.C. 112, first paragraph, enablement and rejections over the reference of Al-Soud et al.

Information Disclosure Statement

6. The information disclosure statements (IDS) submitted on November 30, 2006 and February 20, 2007 were filed after the mailing date of the non-final office action on October 18, 2006. The

submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Response to Arguments

7. Applicant's arguments filed February 20, 2007 have been fully considered but they are not persuasive.

A) Regarding the rejection of claim 39 under 35 U.S.C. 103(a) over Demeke et al. and Barnes and the rejection of claims 43 and 44 under 35 U.S.C. 103(a) over Demeke et al. and Barnes in view of Stratagene Catalog, Applicants argue that Demeke et al. teach away from polysaccharides in the amplification reaction since they act as inhibitors. However, Applicants do not claim any particular DNA polymerase or any particular polysaccharide concentration which has the property of enhancing a DNA amplification. Therefore, the polysaccharides have an inherent property of enhancing the polymerization reaction, especially since Applicants did not define what this term means.

The rejections are maintained.

B) Regarding the rejection of claim 39 under 35 U.S.C. 103(a) over Tasa et al. and Barnes, and the rejection of claims 43 and 44 under 35 U.S.C. 103(a) over Tasa et al. and Barnes in view of Stratagene Catalog, Applicants argue that Tasa et al. teach away from having heparin in the amplification reaction since it acts an inhibitor. However, Applicants do not claim any particular DNA polymerase or any particular heparin concentration which has the property of enhancing a DNA amplification. Therefore, the heparin has an inherent property of enhancing the polymerization reaction, especially since Applicants did not define what this term means.

The rejections are maintained.

Claim Rejections - 35 USC § 112 – Scope of Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

9. The specification shall contain a written description of the invention, and of the manner and process of making and using it,

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 16, 18, 31, 34, 36 and 38-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sulfated-fucose-containing polysaccharides, sodium alginate, sodium polyglutamate, sodium polyacrylate and κ carrageenan as PCR activators, does not reasonably provide enablement for dextran sulfate, rhamnan sulfate, dermatan sulfate, heparan sulfate, hyaluronic acid, polyglutamic acids, polyacrylic acids, polyvinyl sulfates, polystyrene sulfates or their salts and heparin as PCR activators. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

> <u>The nature of the invention</u>

The claims are drawn to compositions and kits for performing PCR where heparin or a number of other acidic macromolecular substances is added to enhance PCR. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims encompass the use of heparin or dextran sulfate, rhamnan sulfate, dermatan sulfate, heparan sulfate, hyaluronic acid, polyglutamic acids, polyacrylic acids, polyvinyl sulfates, polystyrene sulfates or their salts to enhance PCR. The claims broadly encompass the use of the method on PCR samples derived from any cell type, ranging from plants to animals to soil microorganisms. The method applies to any PCR inhibitor, which can include DNA itself when too much target is present, as well as plant secondary metabolites and, as will be discussed below, heparin and dextran sulfate themselves are inhibitors, and the behavior of the other substances in amplification reactions such as PCR has not been evaluated.

Quantity of Experimentation

The quantity of experimentation in this area is large since there is significant variability in the efficacy of steps taken to enhance PCR. This experimentation must take into account variables that depend upon the environment in which the DNA is found as well as the age of the DNA sample and the source of the DNA sample. Different inhibitors are present in ancient DNA samples than in modern DNA samples and different PCR inhibitors are present in plants than are present in blood samples or soil samples. Each of these unique sample types would require independent experimentation and screening in order to determine the efficacy and ability of specific compounds to enhance PCR. Such efforts are inventive, unpredictable and difficult undertakings, as shown by the many patents such as Harvey et al. (U.S. Patent 6,168,922) which discusses removal of PCR

inhibitors. The efficacy of any particular compound to enhance PCR of any particular sample would need to be demonstrated. This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The extremely great weight of both the art prior to the priority date and post filing art teaches that heparin itself is a PCR inhibitor, not a PCR enhancement agent. Applicants did not show a single example of performing a PCR amplification in the presence of heparin. The entirety of the prior and post filing date art found in the prior art search teaches the opposite fact. Here are citations regarding the role of heparin in PCR from the patent literature:

Refseth et al. (U.S. 2003/0153028) note "For certain binding ligands such as heparin, dextran sulphate and carrageenan, this may be preferred as the sulphate group may inhibit the PCR reaction." (see paragraph 233).

Gocke et al. (U.S. 2003/0143600) notes "Since heparin may interfere with PCR, use of heparinized blood may require pretreatment with heparinase." (see paragraph 49).

Helftenbein (U.S. 2003/0143566) notes "Heparin is, for example, a generally known inhibitor of the PCR." (see paragraph 6).

Merigan et al. (U.S. 2003/0118986) notes "It should be noted that heparin appears to have an inhibitory effect on gene amplification via PCR." (see paragraph 21).

Peters (U.S. 2003/0092135) teaches that polyanions themselves are inhibitory to PCR, noting "Acid polyanionic polysaccharides have been characterized as the major PCR inhibitor in plant DNA isolations (Demeke et al., 1992), whereas sulfated polysaccharides, such as dextran

sulfate and heparin were identified as potent PCR inhibitors contaminating DNA preparations from blood cells (Al-Soud et al., 2001). Sulfated polysaccharides in particular show a broad spectrum of inhibition against a variety of DNA-modifying enzymes including Polynucleotide Kinase (Wu et al., 1971), restriction endonucleases (Do et al., 1991) and retroviral reverse transcriptases (Moelling et al., 1989). Although the inhibitory effect of polyanions and sulfated polysaccharides in particular has been studied for many years, the exact mechanism is not known (see paragraph 21)."

Matveld et al. (U.S. Patent 6,348,336) note "The most common PCR inhibitors include heme, heparin, metal ion chelators such as EDTA, and the like. Indeed, many samples are routinely collected in heparin, and it has been estimated that as much as 10% of the total sample population contains at least one form of PCR inhibitor (See column 2, lines 47-51)."

Persing (U.S. Patent 6,087,097) notes "Heparin tubes (green-top) were not used, since they inhibit PCR (see column 7, see lines 66-67)."

Lacroix et al. (U.S. Patent 5,795,722) note "Blood serum is collected and prepared according to methods known in the art, with the exception that heparin is not to be used as an anti-coagulant because it inhibits PCR (see column 12, lines 52-54)."

Burckhardt (U.S. Patent 5,501,963) notes "Israeli et al. (Nucleic Acids Research 19:6051 (1991)) describe the amplification by PCR of RNA which was isolated from frozen heparin-treated whole blood by extraction after conversion of the RNA into cDNA. Israeli demonstrate that the difficulties in conducting PCR were due to the heparin. Only when the isolated RNA was treated with heparinase before transcribing into cDNA, was the PCR successful (see column 2, lines 15-23)."

In addition to these patents, there is abundant prior art literature which shows that heparin is a PCR inhibitor itself. For example, Wang et al. (J. Clin. Microbiol., vol. 30, pp. 750-753, 1992) teach "We have confirmed that heparin interferes with the HCV PCR assay and should not be used as the anticoagulant in specimen collection when detection of HCV RNA is to be undertaken (see page 752, column 1)".

Holodney et al. (J. Clin. Microbiol., vol. 29, pp. 676-679, 1991) note "Here we define and quantitate the inhibitory effect of heparin on PCR by using an enzyme-linked affinity assay for PCR product detection and quantitation (see page 676, column 1)". Holodney et al. conclude the analysis by noting ""In conclusion, our findings demonstrate that heparin can inhibit gene amplification and may not be removed after nucleic acid extraction and suggest that blood samples for PCR should be collected in ACD or EDA (see page 679, column 1)".

Finally, Poli et al. (PCR Meth. Appl., vol. 2, pp. 356-358, 1993) note (page 356, first paragraph): "Blood samples collected with heparin as anticoagulant have been shown to yield decreased quantities of DNA, and an inhibitory effect of this anticoagulant on PCR has been demonstrated."

Therefore, the great weight of both the prior and post filing date art, in both the patent and non-patent literature, teach that addition of heparin or other polyionic compounds does not reduce inhibition as claimed in this application, but that heparin itself is a PCR inhibitor. The examiner did not find a single prior art patent or non-patent literature reference that yielded a different conclusion. Thus, the ordinary practitioner would not expect heparin to function to reduce inhibition of PCR in view of the teachings in the art that heparin is itself a PCR inhibitor. Further, one of ordinary skill in the art would not conclude that any polyionic acidic polymer can be used to enhance PCR amplification.

Working Examples

The specification has no working examples which show that heparin enhances PCR. The specification has no working examples showing enhancement of PCR amplification by the following substances: dextran sulfate, rhamnan sulfate, dermatan sulfate, heparan sulfate, hyaluronic acid, polyglutamic acids, polyacrylic acids, polyvinyl sulfates, polystyrene sulfates or their salts.

Guidance in the Specification.

The specification teaches that acidic macromolecular compounds can be used to enhance amplification, but shows that only the following substances actually do: sulfated-fucose-containing polysaccharides, sodium alginate, sodium polyglutamate, sodium polyacrylate and κ carrageenan.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability and the teaching by ten patent documents and three non-patent references which all uniformly teach that heparin and polyanions are PCR inhibitors, support the conclusion of undue experimentation. The specification provides one with little written description or guidance that leads one to overcome the art recognized fact that heparin and other polyanions are themselves PCR inhibitors. One of skill in the art cannot readily anticipate how to overcome the extensive and complete teaching by the art that heparin is a PCR inhibitor and cannot enhance PCR amplification. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the negative teachings in the prior art

balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 16, 18, 40-42 and 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Al-Soud et al. (Applied Env. Microbiol., vol. 64, pp. 3748-3753, October 1998), as evidenced by Wikipedia ("Heparan Sulfate", April 21, 2007).

Regarding claims 16 and 18, Al-Soud et al. teach a composition comprising a DNA polymerase or two DNA polymerases, one of which has a 3'-5' exonuclease activity and one of which does not and components necessary for DNA synthesis using a polymerase, as well as diluted minced pork meat (page 3749, paragraphs 2-5). Al-Soud et al. do not specifically teach heparan sulfate. However, as evidenced by Wikipedia, heparan sulfate is present in all animal tissues. Therefore, by teaching polymerization reaction with meat solutions Al-Soud et al. inherently teach polymerization in the presence of heparan sulfate.

Regarding claim 18, Al-Soud et al. teach using two different DNA polymerases (page 3749, second paragraph) and polymerases with 3'-5'exonuclease activity (e.g., Pwo) and without the 3'-5' exonuclease activity (e.g. Taq polymerase) (page 3749, second paragraph).

Regarding claim 40, Al-Soud et al. teach a 50 mL reaction mixture (page 3749, second paragraph), and they teach adding meat homogenate concentrations to the final volume of 20, 2,

0.2, 0.1, 0.07, 0.05 and 0.04% (page 3749, fifth paragraph). Therefore, assuming meat density of 1g/cm3, or 1 mg/μl, a ten-fold dilution would have a density of 100 μg/μl. Therefore, in a 25 μl reaction of 20% solution, there would be 5 μl of the meat extract, or 500 micrograms. In a similar manner, a 0.04% reaction would have 0.01 μl of the meat extract, or 1 microgram total of meat. Since the meat is not 100% heparan sulfate, the reactions would inherently contain the claimed amounts of heparan sulfate.

Regarding claims 41, 42 and 45, Al-Soud et al. teach *Thermococcus litoralis*-derived DNA polymerase, *Thermococcus acquaticus*-derived DNA polymerase, Taq DNA polymerase and Pyrococcus-derived (Pwo) polymerase (page 3749, second paragraph; Table 1, 2).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Demeke et al. (Biotechniques, vol. 12, pp. 332, 334, 1992; cited in the IDS and in a previous office action) and Barnes (U.S. Patent No. 5,436,149 A; cited in a previous office action).

A) Demeke et al. teach DNA synthesis reaction compositions comprising Taq DNA polymerase and one of the following polysaccharides: carrageenan, pectin and dextran sulfate, together with reaction components necessary for DNA synthesis (Abstract; page 332, second paragraph; Table 1).

B) Demeke et al. do not teach a polymerase having 3'-5' exonuclease activity.

C) Barnes teaches a composition comprising two DNA polymerases, one with 3'-5' exonuclease activity and one without such activity (col. 3, lines 62-67; col. 4, lines 1-11; col. 16, lines 55-61).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used two polymerases with different 3'-5' exonuclease activities of Barnes in the composition of Demeke et al. The motivation to do so, provided by Barnes, would have been that using such polymerase combination allowed amplification of long DNA targets (col. 16, lines 55-61).

15. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tasa et al. (Meth. Mol. Cel. Biol., vol. 5, pp. 122-124, 1995; cited in the IDS and in a previous office action) and Barnes (U.S. Patent No. 5,436,149 A; cited in a previous office action).

A) Tasa et al. teach a DNA synthesis reaction comprising a Taq DNA polymerase and heparin together with reaction components necessary for DNA synthesis (Abstract; page 123, second paragraph and paragraph entitled "Methodology").

B) Tasa et al. do not teach a composition comprising a DNA polymerase with 3'-5' exonuclease activity.

C) Barnes teaches a composition comprising two DNA polymerases, one with 3'-5' exonuclease activity and one without such activity (col. 3, lines 62-67; col. 4, lines 1-11; col. 16, lines 55-61).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used two polymerases with different 3'-5' exonuclease activities of Barnes in the composition of Tasa et al. The motivation to do so, provided by Barnes, would have been that using such polymerase combination allowed amplification of long DNA targets (col. 16, lines 55-61).

16. Claims 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Demeke et al. (Biotechniques, vol. 12, pp. 332, 334, 1992; cited in the IDS and in a previous office action) and Barnes (U.S. Patent No. 5,436,149 A; cited in a previous office action), as applied to claim 39 above, and further in view of Stratagene catalog (page 39, 1988; cited in a previous office action).

A) Demeke et al. and Barnes et al. teach the reaction composition of claim 39, but they do not teach kits.

B) Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the compositions of Demeke et al. and Barnes et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantitites of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantitites you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

17. Claims 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasa et al. (Meth. Mol. Cel. Biol., vol. 5, pp. 122-124, 1995; cited in the IDS and in a previous office action)

and Barnes (U.S. Patent No. 5,436,149 A; cited in a previous office action), as applied to claim 39 above, and further in view of Stratagene Catalog (page 39, 1988; cited in a previous office action).

A) Tasa et al. and Barnes et al. teach the composition of claim 39, but do not teach kits.

B) Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the compositions of Tasa et al. and Barnes et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantitites of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantitites you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998);

In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 16, 18, 31, 36, 39 and 43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-17 of copending Application No. 10/435,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 10, 13, 14 and 17 of the 10/435,633 application anticipate claims 16 and 31 of the instant application, whereas claims 11, 12, 15 and 16 anticipate claims 18, 36, 39 and 43 of the instant application.

Specifically, claim 10 of the 10/435,633 application is drawn to a kit for carrying out a DNA synthesis method with a shortened time period for DNA synthesis by polymerase chain reaction (PCR), comprising:

(a) a DNA polymerase, of which amount per 1 reaction is 4 to 20 U as dNTPs-incorporating activity per 50 μL of a reaction mixture;

(b) at least one substance enhancing the DNA-synthesizing activity selected from the group consisting of sulfated-fucose-containing polysaccharides, dextran sulfate, carrageenan, heparin, rhamnam sulfate, chondroitin-sulfate, dermatan sulfate (chondroitin sulfate B), heparin sulfate, hyaluronic acid, alginic acid, pectin, polyglutamates, polyacrylates, polyvinyl sulfates, polystyrene sulfates, a 15-deoxyspergualin compound represented by the following general formula

(I), degraded products of said 15-deoxyspergualin, and a salt thereof, wherein said degraded products of said 15-deoxyspergualin are any compounds represented by any of the general formulas (II), (III) and (IV), and

(c) a PCR reagent.

Claim 14 is drawn to a composition comprising:

(a) a DNA polymerase, of which amount per 1 reaction is 4 to 20 U as dNTPs-incorporating activity per 50 μL of a reaction mixture;

(b) at least one substance enhancing the DNA-synthesizing activity selected from the group consisting of sulfated-fucose-containing polysaccharides, dextran sulfate, carrageenan, heparin, rhamnam sulfate, chondroitin-sulfate, dermatan sulfate (chondroitin sulfate B), heparin sulfate, hyaluronic acid, alginic acid, pectin, polyglutamates, polyacrylates, polyvinyl sulfates, polystyrene sulfates, a 15-deoxyspergualin compound represented by the following general formula (I), degraded products of said 15-deoxyspergualin, and a salt thereof, wherein said degraded products of said 15-deoxyspergualin are any compounds represented by any of the general formulas (II), (III) and (IV), and

(c) a PCR reagent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
5/11/07